



# **PCT**

#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

	<u> </u>		
Applicant's or agent's file reference BLOcp226/107	FOR FURTHER ACTION		cation of Transmittal of International Examination Report (Form PCT/IPEA/416)
International application No. PCT/FR2003/002010	International filing date (day/ 27 juin 2003 (27.06		Priority date (day/month/year) 28 juin 2002 (28.06.2002)
International Patent Classification (IPC) or n C12N 5/06	ational classification and IPC		
Applicant	INSTITUT PAST	EUR	
and is transmitted to the applicant ac  2. This REPORT consists of a total of  This report is also accompaniamended and are the basis for	cording to Article 36.  7 sheets, including the day ANNEXES, i.e., sheets on this report and/or sheets contain Administrative Instructions und	ng this cover s f the descripti	national Preliminary Examining Authority sheet. on, claims and/or drawings which have been tions made before this Authority (see Rule
This report contains indications relat	ing to the following items:		,
I Basis of the report II Priority III Non-establishment of IV Lack of unity of inverse of the citations and explanate of the citations are citations	f opinion with regard to novelty ention under Article 35(2) with regard ttions supporting such statemen	to novelty, in	ep and industrial applicability ventive step or industrial applicability;
Date of submission of the demand	Date of	completion of	f this report
20 janvier 2004 (20.01.2	2004)	30 Sep	otember 2004 (30.09.2004)
Name and mailing address of the IPEA/EP	Author	ized officer	
Facsimile No.	Teleph	one No.	

Translation

International application No.

## PCT/FR2003/002010

I. Basis	s of the r	eport	
1. With	h regard t	o the elements of the international application:*	
	the inte	ernational application as originally filed	
	the des	scription:	
	pages	1-17	, as originally filed
ĺ	pages		, filed with the demand
ľ	pages	, filed with the letter of	<del></del> -
	the clai	ims:	
ł	pages	1-9	, as originally filed
ļ	pages	, as amended (together with any	·
	pages		, filed with the demand
İ	pages	, filed with the letter of	
	the drav		
	pages	1/5-5/5	, as originally filed
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These	the lang the lang the lang or 55.3)	to the language, all the elements marked above were available or furnished to this Authority and application was filed, unless otherwise indicated under this item. Its were available or furnished to this Authority in the following language grange of a translation furnished for the purposes of international search (under Rule 23.1(b)) grange of publication of the international application (under Rule 48.3(b)).  Grange of the translation furnished for the purposes of international preliminary examinations.	y in the language in which which is: ). on (under Rule 55.2 and/
		ed in the international application in written form.	
		gether with the international application in computer readable form.	
		ed subsequently to this Authority in written form.	
	furnishe	ed subsequently to this Authority in computer readable form.	
	The sta	atement that the subsequently furnished written sequence listing does not go beyon ional application as filed has been furnished.	nd the disclosure in the
	The star	tement that the information recorded in computer readable form is identical to the writinished.	tten sequence listing has
4.	The ame	endments have resulted in the cancellation of:	
	ti	he description, pages	
		he claims, Nos.	
		he drawings, sheets/fig	
5.	This repo	ort has been established as if (some of) the amendments had not been made, since they have disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**	ve been considered to go
* Replace in this and 70	s report	neets which have been furnished to the receiving Office in response to an invitation under as "originally filed" and are not annexed to this report since they do not contain to	Article 14 are referred to amendments (Rule 70.16
** Any re	placemer	nt sheet containing such amendments must be referred to under item 1 and annexed to this r	report.



International application No.

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n	J. Non-	-establishment of opinion with regard to novelty, inventive step and industrial applicability
1	. The c	questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be trially applicable have not been examined in respect of:
		the entire international application.
	$\boxtimes$	claims Nos. 1-4, 7 (industrial application)
	becaus	se:
	$\boxtimes$	the said international application, or the said claims Nos. 1-4, 7 (see separate sheet) relate to the following subject matter which does not require an international preliminary examination (specify):
		the description, claims or drawings (indicate particular elements below) or said claims Nosare so unclear that no meaningful opinion could be formed (specify):
		the claims, or said claims Nos are so inadequately supported by the description that no meaningful opinion could be formed.
_		no international search report has been established for said claims Nos
2. 1	A mean sequen	ningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid ace listing to comply with the standard provided for in Annex C of the Administrative Instructions:
,		the written form has not been furnished or does not comply with the standard.
1		the computer readable form has not been furnished or does not comply with the standard.

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III

Claims 1-4 and 7 relate to methods for the treatment of the human or animal body by surgery. As a result, no opinion will be established with respect to the industrial applicability of the subject matter of these claims (PCT Rule 67.1(iv)).

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Reasoned statement under Article citations and explanations supporti	ng such statement	elty, inventive step or industrial applical	bility;
Statement			
Novelty (N)	Claims	2, 5	YES
	Claims	1, 3, 4, 6-9	NO
Inventive step (IS)	Claims		YES
	Claims	1-9	NO
Industrial applicability (IA)	Claims	5, 6	YES
	Claims		NO.

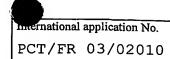
2. Citations and explanations

The present report mentions the following documents cited in the search report:

- D1: DIMARIO JOSEPH X ET AL: "Differences in the developmental fate of cultured and noncultured myoblasts when transplanted into embryonic limbs" EXPERIMENTAL CELL RESEARCH, vol. 216, no. 2, 1995, pages 431-442, XP002264234 ISSN: 0014-4827;
- D2: WO 01 36482 A (MIGNONE JOHN; COLD SPRING HARBOR LAB (US); ENIKOLOPOV GRIGORI N (US)) 25 May 2001 (2001-05-25) (cited in the application);
- D3: POUZET BRUNO ET AL: "Intramyocardial transplantation of autologous myoblasts: Can tissue processing be optimized?" CIRCULATION, vol. 102, no. 19 Supplement, 7 November 2000 (2000-11-07), pages III.210-III.215, XP002264235 ISSN: 0009-7322.

Novelty (PCT Article 33(2))

The subject matter of claims 1, 3, 4 and 6-9 lacks novelty



over documents D1, D2 and D3:

D1 describes a method for transplanting chicken or quail myoblasts of embryonic, foetal or adult origin into limb buds of chicken embryos. According to said method, the muscle areas are first chopped, then exposed to enzymatic digestion (collagenase and trypsin). The freshly isolated myoblasts are transplanted directly. Unlike the fibroblasts that are cultured prior to transplantation, said myoblasts are capable of forming numerous muscle fibres with long-term persistence (D1, the abstract; page 432, column 1, paragraph 1 to column 2, paragraph 2; page 440, last paragraph to page 441, last paragraph).

The stem cells or cell compositions produced using the method described in D1, as well as the transplantation method described in D1, are prejudicial to the novelty of claims 6-9.

D2 describes a method for transplanting neural stem cells, in which the cells are not precultured. (Mouse) brain tissue is placed in a specific medium (DMEM/F12) and dissociated, firstly by adding trypsin then by using mechanical means (pipette). The cells are collected by means of centrifugation, then stored in Hank's Buffered Salt Solution (HBSS) before being injected into a rat brain. After one week, it was possible to note the survival of the cells and their incorporation into the brain (D2, page 1, lines 12-26; page 21, lines 22-27; example 8). D2 discloses all of the steps of the method of claim 1 and is, as a result, prejudicial to the novelty of claims 1, 3 and 4. The stem cells or cell compositions as well as the transplantation method disclosed in D2 deprive claims 6-9 of novelty.

myoblasts, in which the muscle tissue is chopped then exposed to enzymatic dissociation. The cells are collected by means of sedimentation and centrifugation, then kept in a specific culture medium consisting of F12 with 20% of FBS added thereto, and containing basic fibroblast growth factor (bFGF) (D2, page III-211, "Cell culture methodology", column 1, last paragraph to column 2, line 4). The Examining Authority considers that the cell composition and the stem cells produced in D3 deprive claims 6, 8 and 9 of novelty.

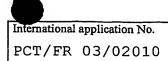
#### Inventiveness (PCT Article 33(3))

The subject matter of <u>claims 2 and 5</u> does not involve an inventive step in view of D1 or D2, for the following reasons:

D1 and D2 describe the production of muscle or neural stem cells and the transplantation of same into an animal without carrying out a preculture step. Even though D1 or D2 do not explicitly define a specific medium for preserving the cells before carrying out the transplantation step, defining the properties of such a medium is within the abilities of a person skilled in the art. It follows that the method as per claim 2 is not considered to be inventive.

Furthermore, D1 and D2 disclose stem cells such as the ones claimed in the present application (see above) and mention the therapeutic use of stem cells in general (D1, page 441, last paragraph; D2, page 6, line 31). As a result, the therapeutic use of





the stem cells produced in D1 or D2 would be obvious to a person skilled in the art and does not involve an inventive step.

2. It is brought to the applicant's attention that, in so far as the subject matter of the claims relates specifically to the grafting of <a href="mailto:skeletal muscle">skeletal muscle</a> cells to the <a href="mailto:myocardium">myocardium</a> without any pre-expansion of said cells in <a href="mailto:in-vitro">in-vitro</a> culture, said subject matter is considered to be novel and inventive in relation to the documents cited in the international search report.